8. One comment states that there is no evidence in the administrative record that smokeless tobacco manufacturers add compounds for the purpose of affecting nicotine absorption into the bloodstream.

The Agency disagrees with this comment. As discussed in section II.D.2.a., above, there is substantial evidence in the record that the manufacturers add buffering agents to raise the pH levels in smokeless tobacco, which has the effect of increasing nicotine absorption.

9. In the Jurisdictional Analysis, FDA reported that smokeless tobacco delivers nicotine at its most rapid rate within 5 minutes after placing the product in the mouth.[1083] Blood levels then continue to rise while the smokeless tobacco product is kept in the mouth.[1084] One smokeless tobacco industry comment contends that this FDA finding is false and misleading. According to the comment, the Agency relied on in vitro data that do not purport to simulate bioavailability in users. In addition, the comment states that the Agency did not cite any evidentiary support for its statement that the bolus dose results in peak pharmacological concentrations in users, maintained by slow continued release of nicotine from the product.

The Agency disagrees that its statement concerning the bolus dose of nicotine delivered by smokeless tobacco is false or misleading. The administrative record contains in vitro data demonstrating that when smokeless tobacco was placed in simulated saliva, a significant amount of nicotine was released from the products within the first 5 seconds.[1085]

[1083] Benowitz N, Porchet H, Sheiner L, et al., Nicotine absorption and cardiovascular effects with smokeless tobacco use: comparison with cigarettes and nicotine gum, *Clinical Pharmacology and Therapeutics* 1988;44:23-28, at 25. *See* AR (Vol. 12 Ref. 134).

[1084] *Id.* at 24, fig. 1.

[1085] Memorandum from Ciolino L, *Moist Snuff Nicotine Release Studies* (Sep. 28, 1994), at table IV.A. *See* AR (Vol. 30 Ref. 500-2).

This study provides strong evidence that a significant amount of nicotine is available for absorption within the first 5 seconds of use.

Additionally, the administrative record includes an in vivo pharmacokinetic study consistent with these in vitro results. This study concluded that rate of nicotine absorption peaks about 5 minutes after placing oral snuff and chewing tobacco in the mouth.[1086]

Thus, the Agency provided both *in vivo* and *in vitro* data independently demonstrating that peak pharmacologic concentrations of nicotine are delivered within 5 minutes of placing smokeless tobacco in the mouth. The comment provided no evidence to rebut this conclusion.

b. Comments on the Graduation Process

1. Two smokeless tobacco industry comments contend that persuasive evidence of a graduation process would have come from a survey of smokeless tobacco users showing that switching is unidirectional (i.e., that when a user switches, he always switches from a pouch to a loose tobacco product and from a lower to a higher pH product), but that FDA failed to present such evidence. The comments claim that consumer demographic data demonstrate that there is "significant brand loyalty" and that many smokeless tobacco users stay with the brand they first choose. Furthermore, the comments claim that any switching that does occur does not indicate any patterns, and that social and other factors cause smokeless tobacco users to choose their own brands.

[1086] Benowitz N, Porchet H, Sheiner L, *et al.*, Nicotine absorption and cardiovascular effects with smokeless tobacco use: comparison with cigarettes and nicotine gum, *Clinical Pharmacology and Therapeutics* 1988;44:23-28, at 26. *See* AR (Vol. 12 Ref. 134).

II.D.4.

Contrary to the comments, the evidence in the record does in fact demonstrate a clear pattern of switching from brands of smokeless tobacco that deliver low levels of nicotine to brands that deliver higher levels of nicotine. As discussed in section II.D.2., above, an analysis of data from CDC's 1993 Teenage Attitudes and Practices Survey (TAPS) and a follow-up study from the 1989 TAPS shows that most brand switching involves switching from products with low nicotine delivery to products with higher nicotine delivery.

The comments do not provide data or any other documentation to the Agency to support the claim that there is no pattern to brand switching. Without any such evidence to support its claim, the smokeless tobacco industry has not provided an adequate basis to rebut the Agency's findings.

2. UST denies that it uses a graduation strategy in the manufacture and marketing of its products. Specifically, the UST comment states:

> As best as U.S. Tobacco can now determine, the term "graduation process" as used in the early 1980s (1) did not relate to increasing levels of nicotine and pH; (2) did not drive the company's marketing strategies; and (3) is contradicted by consumer behavior in the marketplace.[1087]

The Agency does not find UST's position to be credible. Contrary to UST's assertions, its products do deliver graduated levels of nicotine, *see* section II.D.2.a., above; UST's marketing strategies do target low-nicotine products for new users and high-nicotine products for experienced users, *see* section II.D.2.c., above; and consumers do shift from low-nicotine products to high-nicotine products. *See* section II.D.2.b., above. Moreover, senior UST officials, including the president of UST, and other UST documents do use the

[1087] U.S. Tobacco Company, Comment (Jan. 2, 1996), at 32. *See* AR (Vol. 529 Ref. 98).

phrase "graduation process" to describe UST's marketing approach. *See* section II.D.2.c., above.

3. UST alleges that FDA's reliance on various UST documents and statements made by UST executives is ill-founded. UST claims that, among other things, the Agency took statements out of context; the statements were not representative of UST's position; and the Agency improperly relied on statements, documents, and offers of proof from the plaintiff's attorneys in a product liability suit.

The Agency believes that all of the documents and statements speak for themselves and fully support the position taken in the Jurisdictional Analysis. A summary of those comments and the Agency's response follows:

a. In the Jurisdictional Analysis, the Agency referred to several statements made by a UST senior vice-president for marketing which demonstrate that UST understands the relationship between the pH of its products and nicotine delivery. UST states that the Agency mischaracterized the comments and failed to mention that the marketing executive disclaimed his expertise with respect to pH and nicotine in a prior exchange within the cited deposition.

While the Agency did not mention the prior exchange in the Jurisdictional Analysis, this omission does not affect the meaning of the relevant passages. As the record shows, this senior vice-president for marketing acknowledged his understanding that as the pH of the smokeless tobacco product is lowered, the rate of nicotine absorption by the user is also lowered:

> Q. Mr. Lindqvist, is it your understanding that as the pH of the product is lowered, that the rate of absorption of nicotine by the user is also lowered?

A. That would be my understanding, yes.[1088]

The record also shows that this senior vice president participated in discussions with other senior level executives within the company about product development and specifically made suggestions for pH levels for those products that reflect his knowledge of the relationship of pH to the nicotine strength of the product. For instance, in discussing the specifications for a "premium project," he recommended that UST set "*pH at the level of Copenhagen or higher.*"[1089] These statements demonstrate knowledge of the relationship of pH and nicotine delivery.

b. In the Jurisdictional Analysis and in section II.D.2.c., above, the Agency cites several UST documents that referred to the "Lotus Project." These documents disclosed the company's intent to produce products with varying amounts of nicotine and to develop a low nicotine product especially for new users. UST states that some of the comments referred to were just "one individual's preliminary thoughts"[1090] about a low-nicotine product. Further, UST states that the Lotus Project documents refer to a Swedish marketing campaign by a foreign smokeless tobacco manufacturer, not a project planned for the United States or any other market by U.S. Tobacco.

The UST documents in question speak for themselves. The "one individual's preliminary thoughts" were those of the president of UST's smokeless tobacco foreign

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[1088] Deposition of Erik Lindqvist, *Marsee v. U.S. Tobacco,* Civil Action No. 84-2777R (W.D. Ok. 1986) Transcript of jury trial proceedings at 1668. *See* AR (Vol. 29 Ref. 489-2).

[1089] U.S. Tobacco Company memo from Erik Lindqvist (Sep. 22, 1981) (emphasis added). This document was discussed in the trial transcript in *Marsee v. U.S. Tobacco* at 1668-1669. *See* AR (Vol. 29 Ref. 489-2).

[1090] Joint Comments of the Smokeless Tobacco Manufacturers (Jan. 2, 1996), at 24. *See* AR (Vol. 526 Ref. 95).

subsidiary and were made to the president of UST in a memorandum written on UST letterhead and labeled "Intra-Company Correspondence."[1091] Contrary to UST's comment, the president of UST expressly stated that the Swedish smokeless tobacco company and UST were "cooperat[ing] on this project" and that "he wanted a Lotus product for the U.S. market."[1092] Suggestions for product development made by corporate executives carry significant weight and cannot be dismissed as one individual's preliminary thoughts. *See Ezold v. Wolf*, 983 F.2d 509, 546 (3d. Cir. 1992). Furthermore, UST acknowledges that "[s]uch a portion pack product, intended to appeal to cigarette smokers, was ultimately marketed in the U.S. under the brand name Skoal Bandits."[1093]

c. In the Jurisdictional Analysis and in section II.D.1. above, the Agency cited as a UST document that posed "Potential Questions and Answers" about UST's introduction of Skoal Bandits in a foreign market.[1094] One question the company assumes consumers will ask is, "How much nicotine does it contain? Is it absorbed?"[1095] The company replies that the product contains about as much nicotine as an average cigarette and that "[t]he nicotine is absorbed, giv[ing] satisfaction to the smoker."[1096] The Agency stated that the document

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[1091] Intra-company correspondence from Watson WW (president, Scandia Internationals) to Bantle LA (president, U.S. Tobacco Company) (Jun. 2, 1972), from *Marsee v. U.S. Tobacco*, trial exhibit 158. *See* AR (Vol. 30 Ref. 505-2).

[1092] Minutes from meeting in Greenwich at Bantle LA's office (Jul. 18, 1972), at 1, from *Marsee v. U.S. Tobacco*, trial exhibit 159. *See* AR (Vol. 30 Ref. 505-3).

[1093] Joint Comments of the Smokeless Tobacco Manufacturers (Jan. 2, 1996), at 24. *See* AR (Vol. 526 Ref. 95).

[1094] Potential Questions and Answers, submitted in *Marsee v. U.S. Tobacco*, at 1. *See* AR (Vol. 30 Ref. 509).

[1095] *Id.*

[1096] *Id.*

demonstrates the manufacturer's intent to provide nicotine for absorption and thereby provide "satisfaction" to the smokeless tobacco user. UST argues that there is no suggestion by FDA that any of the statements contained in the document were ever communicated to the public, within or outside of the United States, and therefore that this document is irrelevant to establishing intended use.

FDA disagrees. This document is relevant to establishing the intent of the manufacturer, whether or not the information within the document was ultimately communicated to the public. The evidence relevant to establishing intended use is discussed in greater detail in sections II.C.1. and II.C.2.e., above, and II.E., below. As described therein, the manufacturer's intent may be demonstrated by company documents, regardless of whether the documents are disclosed to the public. In this case, the questions and answers on nicotine content and absorption demonstrate UST's knowledge of nicotine's effects on users of smokeless tobacco and the company's awareness of users' desire for satisfying doses of nicotine.

d. UST states that FDA relies on documents from a product liability lawsuit (*Marsee v. UST*), as well as sections of the trial transcript, and contends that these are distortions and mischaracterizations from plaintiff's attorneys. The comments also state that FDA relied on unsubstantiated statements made by the plaintiff's attorney in that case as part of an offer of proof.

In several instances, the Agency cited portions of a trial transcript that recorded the questioning of a senior UST official. The statements relied on by FDA were made by the UST official for a deposition or as part of the trial proceedings under penalty of perjury. The

Agency does not have any reason to believe that the testimony was fraudulent, nor has the comment suggested that it was.

The Agency agrees that some of the quotes cited in the Jurisdictional Analysis and in this document were entered into the trial record of *Marsee* as an offer of proof. None of these quotes, however, are essential to FDA's analysis. Moreover, the Agency does not have any reason to believe that the attorneys mischaracterized the statements made in the documents, nor has the comment offered any such reason. The comment has thus provided no persuasive basis on which to reject this evidence.

e. UST argues that the Agency misinterprets the use of the terms "strength" and "nicotine satisfaction," as used in UST internal company documents. The company states that there is no evidence to support FDA's contention that "strength" refers to the delivery of nicotine. The comment further states that "satisfaction" is highly subjective and means something different to different people and that "nicotine satisfaction," as used in the smokeless tobacco company documents, refers to "taste."

The evidence shows that "strength," as used in various UST company documents, refers to nicotine delivery. Express statements made by UST officials refer to "strength" of nicotine and differentiate both "strength" and "satisfaction" from "taste" of the product.[1097] As described in section II.D.2.c., above, for instance, one UST document specifically urged UST to develop products with "three different . . . strengths of nicotine."[1098] Another UST

[1097] *The Lotus Project*, attached to minutes from a meeting in Greenwich at Bantle LA's office (Jul. 18, 1972), from *Marsee v. U.S. Tobacco*, trial exhibit 159. *See* AR (Vol. 30 Ref. 505-3).

[1098] Intra-company correspondence from Watson WW (president, Scandia Internationals) to Bantle LA (president, U.S. Tobacco Company) (Jun. 2, 1972), at 2, from *Marsee v. U.S. Tobacco*, trial exhibit 158. *See* AR (Vol. 30 Ref. 505-2).

document states: "Our sales and marketing groups have asked for a W.B. type chew with *less strength* saying the present product contains *too much nicotine* for the type chewer to whom they would like to direct the sale of such a product."[1099]

Another UST document explicitly links nicotine with satisfaction, stating that "virtually all tobacco usage is based upon nicotine, 'the kick', *satisfaction.*"[1100]

Based on these statements and other statements in the record, the evidence in the record supports the Agency characterization of strength and satisfaction.

4. UST argues that there is nothing in the record to support FDA's assertion that its advertisements encourage established users to graduate to higher nicotine delivery products.

The Agency disagrees with this comment. UST's advertisements specifically promote graduation to higher-nicotine products. Low-nicotine products are marketed for new users, sometimes referred to as "You Guys Just Starting Out." In contrast, advertisements for high-nicotine products use slogans like "Sooner or Later It's Copenhagen" that promote graduation to the higher nicotine product. *See* section II.D.2.c., above.

Moreover, as discussed in section II.D.2.c, above, a UST chart depicts the graduation process as a bullseye and shows how UST's marketing strategies encourage graduation.

[1099] *Health Effects of Smokeless Tobacco: Hearings Before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, U.S. House of Representatives*, 103d Cong. 2d Sess. 61 (Nov. 29, 1994) (emphasis added). *See* AR (Vol. 710 Ref. 4).

[1100] Deposition of Erik Lindqvist, *Marsee v. U.S. Tobacco*, transcript of jury trial proceedings, at 1662 (emphasis added). *See* AR (Vol. 29 Ref. 489-2).

c. Other Comments

1. One comment argues that FDA intends to assert jurisdiction over the entire moist snuff industry by relying exclusively on information about one company, UST, without any information in the record about other companies.

FDA disagrees with this comment. In section II.A., above, FDA has concluded that the pharmacological effects and uses of smokeless tobacco would be foreseeable to any reasonable manufacturer of smokeless tobacco. On the basis of these foreseeable consequences, FDA has found that smokeless tobacco manufacturers intend to affect the structure and function of the body. This basis for establishing jurisdiction applies equally to all the smokeless tobacco manufacturers.

In section II.B., above, FDA has established that the intended use of smokeless tobacco is to affect the structure and function of the body based on the actual consumer use of smokeless tobacco. This finding applies equally to all the smokeless tobacco manufacturers.

In this section, FDA has found that the smokeless tobacco manufacturers intend to affect the structure and function of the body based on the statements, research, and actions of the manufacturers. Contrary to the comment, the record contains substantial evidence of the statements, research, and actions of smokeless tobacco manufacturers other than UST.

First, the evidence shows that the major smokeless tobacco manufacturers have knowledge of the pharmacological effects of nicotine, one of the major constituents of smokeless tobacco. Some of the smokeless tobacco manufacturers, like UST and Brown & Williamson, have conducted their own extensive research into nicotine pharmacology. All the major smokeless tobacco companies have acquired knowledge of nicotine pharmacology